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Beth A. Burrous  
FOLEY & LARDNER  
Washington Harbour, Suite 500  
3000 K Street, N.W.  
Washington, DC 20007-5109

EXAMINER

COLEMAN, BRENDA LIBBY

ART UNIT

PAPER NUMBER

1624

DATE MAILED: 01/29/2003

9

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/769,360

Applicant(s)

TANG et al.

Examiner

Brenda Coleman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on Nov 19, 2002
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1, 2, 11, 12, 15-17, 20-28, 31-34, and 37-39 is/are pending in the application.
- 4a) Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 11, 12, 15-17, 20-28, 31-34, and 37-39 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some\* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\*See the attached detailed Office action for a list of the certified copies not received.

- 14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_ 6) ☐ Other:

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### **DETAILED ACTION**

Claims 1, 2, 11, 12, 15-17, 20-28, 31-34 and 37-39 are pending in the application.

This action is in response to applicant's amendment filed November 19, 2002. Claims 3-10, 13, 14 and 36 have been canceled and claims 1, 11, 12, 16, 17, 26-28, 32-34 and 37 have been amended.

#### ***Response to Amendment***

Applicant's arguments filed November 19, 2002 have been fully considered with the following effect:

1. The applicant's amendments are sufficient to overcome the improper Markush rejection of claims 1, 2, 10-12, 16, 26-28, 32-34 and 37-39 of the previous office action which is hereby **withdrawn**.
2. The applicant's amendments are sufficient to overcome the 35 USC § 112, first paragraph rejections of claims 1 and 2 of the previous office action which is hereby **withdrawn**.
3. The applicant's amendments are sufficient to overcome the 35 USC § 112, second paragraph rejections of claims 1, 2, 10-12, 26, 28, 33, 34 and 37-39 of the last office action, which are hereby **withdrawn**.

In view of the amendment dated November 19, 2002, the following new grounds of rejection apply:

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***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1, 2, 11, 12, 15-17 and 20-25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The scope of the method claims 1, 2, 11, 12, 15-17 and 21-25 are not adequately enabled solely based on serine/threonine protein kinase provided in the specification. Claims 1, 2, 11, 12, 15-17 and 21-25 are the method of modulating the function of any and all diseases and/or disorders associated with serine/threonine protein kinase which is not remotely enabled. The scope of claims 1, 2, 11, 12, 15-17 and 21-25 includes diseases and/or disorders not even known at this time which may be associated with serine/threonine protein kinase. While treatment of certain types of cancer have been linked with serine/threonine protein kinase, the art does not recognize use of such modulators as broad based drugs for treating all disorders instantly embraced.

Furthermore, evidence involving a single compound and two types of cancer was not found sufficient to establish the enablement of claims directed to a method of treating seven types of cancer with members of a class of several compounds *In re Buting* 163 USPQ 689. The remarkable advances in chemotherapy have seen the development of specific compounds to treat

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specific types of cancer. The great diversity of diseases falling within the “cancer” category means that it is contrary to medical understanding that any agent (let alone a genus of thousands of compounds) could be generally effective against such diseases. The intractability of these disorders is clear evidence that the skill level in this art is low relative to the difficulty of the task.

There never has been a compound capable of treating cancer generally. There are compounds that treat a range of cancers, but no one has ever been able to figure out how to get a compound to treat cancer generally, or even a majority of cancers. Thus, the existence of such a “silver bullet” is contrary to our present understanding in oncology. Even the most broadly effective antitumor agents are only effective against a small fraction of the vast number of different cancers known. This is true in part because cancers arise from a wide variety of sources, such as viruses (e.g. EBV, HHV-8, and HTLV-1), exposure to chemicals such as tobacco tars, genetic disorders, ionizing radiation, and a wide variety of failures of the body’s cell growth regulatory mechanisms. Different types of cancers affect different organs and have different methods of growth and harm to the body, and different vulnerabilities. Thus, it is beyond the skill of oncologists today to get an agent to be effective against cancers generally, evidence that the level of skill in this art is low relative to the difficulty of such a task.

Where the utility is unusual or difficult to treat or speculative, the examiner has authority to require evidence that tests relied upon are reasonably predictive of *in vivo* efficacy by those skilled in the art. See *In re Ruskin*, 148 USPQ 221; *Ex parte Jovanovics*, 211 USPQ 907; MPEP 2164.05(a).

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Patent Protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. Tossing out the mere germ of an idea does not constitute enabling disclosure. *Genentech Inc. v. Novo Nordisk* 42 USPQ2d 1001.

5. Claims 17 and 20-25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The scope of the method claims are not adequately enabled solely based on its modulation of serine/threonine protein kinase provided in the specification. Instant claim language embraces disorders not only for treatment but for **prevention** which is not remotely enabled. It is presumed in the prevention of the diseases and/or disorders claimed herein there is a way of identifying those people who may develop cancer and or [fibrotic] disorders. There is no evidence of record which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disorder claimed herein.

6. Claims 17 and 20-25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The scope of the method claims are not adequately enabled solely based on its modulation of serine/threonine protein kinase provided in the specification. Instant claim

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language embraces any and all disorders which are the result of an "abnormal condition" which is not remotely enabled. The scope of claims 17 and 20-25 includes diseases and/or disorders not even known at this time which falls within the applicants definition of an abnormal condition. While treatment of certain types of cancer have been linked with serine/threonine protein kinase, the art does not recognize use of such modulators as broad based drugs for treating all disorders instantly embraced.

7. Claim 27 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The amendment to the definition of Z' in claim 27, which includes carbon is not described in the specification within the subgenus exemplified in claim 27.

Applicant is required to cancel the new matter in the reply to this Office action.

8. Claims 1, 2, 11, 17, 21-27, 33, 34 and 37-39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The five membered ring which is attached to the quinazoline compounds of formula I at the five position contains a variable A<sub>1</sub> which is defined as carbon, nitrogen, oxygen, and sulfur, however, it is not known how to make and use the compounds of formula I where A<sub>1</sub> is oxygen or sulfur since this would yield compounds where the oxygen and

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sulfur atom has three bonds. Also, the five-membered or six-membered heteroaryl ring formed when  $R_{13}$  and  $R_{14}$  are taken together with  $Z'$ , which is attached to the quinazoline compounds of formula III at the five position contains a variable  $Z'$  which is defined as carbon, oxygen, sulfur, or nitrogen, however, it is not known how to make and use the compounds of formula III where  $Z'$  is oxygen or sulfur since this would yield compounds where the oxygen and sulfur atom has three bonds.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1, 2, 11, 12, 15-17, 20-28, 32-34 and 37-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

- a) Claims 1, 2, 11, 17, 21-27, 33, 34 and 37-39 are vague and indefinite in that it is not known what is meant by the proviso where  $A_1$  is not substituted, since the substituent on the  $A_1$  is the quinazoline ring.
- b) Claims 1, 2, 17, 21-26 and 33 are vague and indefinite in that it is not known what is meant by a quinozaline ring, in the third line of page 4 in claim 1; in the seventh line from the bottom of claim 17; in the fifth line from the bottom of page 10 in claim 26.



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- c) Claims 1, 2, 11, 17, 21-27, 33, 34 and 37-39 are vague and indefinite in that it is not known what is meant by “comprises two carbon atoms of quinozoline ring to which R<sub>3</sub>, R<sub>4</sub>, and R<sub>5</sub> or R<sub>6</sub>, R<sub>7</sub>, R<sub>8</sub>, and R<sub>9</sub> are attached” since R<sub>6</sub>, R<sub>7</sub>, R<sub>8</sub>, and R<sub>9</sub> are not attached to the quinazoline ring.
- d) Claims 11, 27 and 33 are vague and indefinite in that it is not known what is meant by the definition of n which is not in the alternative.
- e) Claim 11 recites the limitation “(v) -OX<sub>7</sub>, where X<sub>7</sub> is selected from the group consisting of hydrogen, saturated or unsaturated alkyl, and a five-membered or six-membered aryl or hetereoaryl ring moiety” in the definition of R<sub>3</sub>, R<sub>4</sub>, R<sub>5</sub>, R<sub>6</sub>, R<sub>7</sub>, R<sub>8</sub> and R<sub>9</sub>. There is insufficient antecedent basis for this limitation in the claim.
- f) Claim 11 is vague and indefinite in that it is not known what is meant by “hetereoaryl” in the definition of X<sub>7</sub>.
- g) Claim 11 recites the limitation “(f) any adjacent R<sub>3</sub>, R<sub>4</sub>, and R<sub>5</sub> or any adjacent R<sub>6</sub>, R<sub>7</sub>, R<sub>8</sub> and R<sub>9</sub> are fused together to form a five-membered.....aryl” in the definition of any adjacent R<sub>3</sub>, R<sub>4</sub>, and R<sub>5</sub> or any adjacent R<sub>6</sub>, R<sub>7</sub>, R<sub>8</sub> and R<sub>9</sub>. There is insufficient antecedent basis for this limitation in the claim.
- h) Claim 11 is vague and indefinite in that it is not known what is meant by “hetereoaryl” in the definition of any adjacent R<sub>3</sub>, R<sub>4</sub>, and R<sub>5</sub> or any adjacent R<sub>6</sub>, R<sub>7</sub>, R<sub>8</sub> and R<sub>9</sub> are fused together.

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- i) Claim 11 recites the limitation "is optionally substituted with one, two, or three alkyl, halogen, trihalomethyl, carboxylate, and ester moieties" in the definition of  $R_{13}$  and  $R_{14}$ . There is insufficient antecedent basis for this limitation in the claim.
- j) Claims 12 and 28 are vague and indefinite in that it is not known what is meant by the definition of Z and n since there are no variables Z and n in formula (V).
- k) Claim 12 recites the limitation " $NX_1X_2$ , where  $X_1$ " in the definition of  $R_1$  and  $R_2$ . There is insufficient antecedent basis for this limitation in the claim. The variables in claim 1 from which claim 12 depends defines  $R_1$  and  $R_2$  as  $NX_2X_3$ .
- l) Claim 12 recites the limitation "benzyl" in the definition of  $R_1$  and  $R_2$ . There is insufficient antecedent basis for this limitation in the claim.
- m) Claim 12 recites the limitation " $NX_3X_4$ , where  $....X_4$ " in the definition of  $R_3$ ,  $R_4$  and  $R_5$ . There is insufficient antecedent basis for this limitation in the claim. The variables in claim 1 from which claim 12 depends defines  $R_3$ ,  $R_4$  and  $R_5$  as  $NX_2X_3$ .
- n) Claims 15 and 20 recite the limitation " $R_3$ ,  $R_4$ ,  $R_5$  and  $R_6$  which are attached to the pyrrole ring" in the structure of formula (X). There is insufficient antecedent basis for this limitation in the claim.
- o) Claims 15 and 20 recite the limitation " $R_3$ ,  $R_4$ ,  $R_5$  and  $R_6$  are independently selected from the group consisting of (i) hydrogen....." with respect to the structure of formula (X). There is insufficient antecedent basis for this limitation in the claim.  $R_3$ ,  $R_4$  and  $R_5$  are substituents of the quinazoline ring in claim 1.

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- p) Claims 16 and 32 are vague and indefinite in that the claims do not end with a period.
- q) Claim 26 is vague and indefinite in that it is missing a paragraph break between (g) and (h) in the definition of R<sub>3</sub>, R<sub>4</sub>, R<sub>5</sub>, R<sub>6</sub>, R<sub>7</sub>, R<sub>8</sub> and R<sub>9</sub>.
- r) Claim 28 is vague and indefinite in that it is not known what is meant by "R<sub>11</sub> and R<sub>12</sub> hydrogen", there are no variables R<sub>11</sub> and R<sub>12</sub> in formula (V).
- s) Claim 34 recites the limitation "said second structure" in the method of synthesizing a compound of claim 26. There is insufficient antecedent basis for this limitation in the claim.
- t) Claim 34 recites the limitation "(f) any adjacent R<sub>3</sub>, R<sub>4</sub>, and R<sub>5</sub> or any adjacent R<sub>6</sub>, R<sub>7</sub>, R<sub>8</sub> and R<sub>9</sub> are fused together to form a five-membered.....aryl" in the definition of any adjacent R<sub>3</sub>, R<sub>4</sub>, and R<sub>5</sub> or any adjacent R<sub>6</sub>, R<sub>7</sub>, R<sub>8</sub> and R<sub>9</sub>. There is insufficient antecedent basis for this limitation in the claim.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

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The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

(f) he did not himself invent the subject matter sought to be patented.

(g) before the applicant's invention thereof the invention was made in this country by another who had not abandoned, suppressed, or concealed it. In determining priority of invention there shall be considered not only the respective dates of conception and reduction to practice of the invention, but also the reasonable diligence of one who was first to conceive and last to reduce to practice, from a time prior to conception by the other.

10. Claims 26-28 and 31-33 are rejected under 35 U.S.C. 102(e, f and g) as being anticipated by Shenoy et al., U.S. Patent Numbers 6,248,771. Shenoy teaches the compounds and compositions of the instant invention where Z', R<sub>13</sub> and R<sub>14</sub> form a pyrrole; R<sup>1</sup> is -NH<sub>2</sub> and R<sup>2</sup> is -NH<sub>2</sub>. See the example at the bottom of column 30.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

11. Claims 26-28 and 31-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shenoy et al., U.S. Patent No. 6,248,771. The generic structure of Shenoy encompasses the instantly claimed compounds (see Formula I, column 5) as claimed herein. The example at the bottom of column 30 differs only in the nature of the R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, R<sub>5</sub> and R<sub>6</sub> substituents. Column 5, lines 15-55 defines the substituents R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, R<sub>5</sub> and R<sub>6</sub> as (i) hydrogen; (ii)

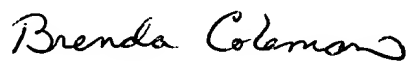
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saturated or unsaturated alkyl; (iii) an aryl optionally substituted with one, two, or three substituents..... Compounds of the instant invention are generically embraced by Shenoy in view of the interchange ability of R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, R<sub>5</sub> and R<sub>6</sub> substituents of the quinazoline ring system. Thus, one of ordinary skill in the art at the time the invention was made would have been motivated to select for example pyridyl or pyrrolylamino as well as other possibilities from the generically disclosed alternatives of the reference and in so doing obtain the instant compounds in view of the equivalency teachings outlined above.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda Coleman whose telephone number is (703) 305-1880. The examiner can normally be reached on Mondays from 8:30 AM to 5:00 PM, on Tuesdays from 8:00 AM to 4:30 PM, on Wednesday thru Friday from 9:00 AM to 5:30 PM.

The fax phone number for this Group is (703) 308-4734 for "unofficial" purposes and the actual number for **OFFICIAL** business is **308-4556**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

  
Brenda Coleman  
Primary Examiner AU 1624  
January 24, 2003